EARLY DETECTION OF MILD COGNITIVE IMPAIRMENT IN PATIENTS WITH ISCHEMIC VASCULAR EVENTS

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ABSTRACT

Evaluation of mild cognitive impairment is important for early management in order to prevent severe dementia. The goal of our study was to assess the cognitive state in patients with ischemic vascular events (first ever stroke or transient ischemic attack).We studied 86 patients who were hospitalized in The Clinic of Neurology from Craiova during the year 2007, for first ever stroke (56 patients) or transient ischemic attack (TIA-32 patients) and also a group composed of 92 control subjects without signs of cerebrovascular disease but with vascular risk factors present. We used for the assessment two scales: Mini Mental State Examination (MMSE) and Cambridge Cognitive Examination (CAMCOG). We made assessment at baseline, after 3 months respectively 6 months. We performed computed tomography in both groups, for a correct diagnosis. At baseline the patient group had a mean MMSE score 27,3 and a mean CAMCOG score 93,9. The control subjects had a mean MMSE score 28,5 and a mean CAMCOG score 96,8. After 6 months the patient group showed a mean MMSE score 25,4 and CAMCOG score 81,9. The control subjects showed a mean MMSE score 26,6 and CAMCOG score 88,95. The patients with cerebrovascular events showed a higher cognitive impairment than the control subjects. Patients with stroke presented a greater cognitive impairment than TIA patients. In subjects with cerebrovascular risk factors we observed the cognitive decline even before the cerebrovascular events became clinically evident.
Key words: cognitive impairment, stroke, TIA, MMSE, CAMCOG

INTRODUCTION

Some older persons may develop mild memory deficites and other cognitive problems that are worse than usually expected due to aging- a condition called Mild Cognitive Impairment. The term of mild cognitive impairment (MCI) refers to a transitional stage between cognitive changes of normal aging and dementia, of both Alzheimer's and vascular type[1]. The disorder can affect many areas of thought and action such as language, attention, judgment, reading and writing. However, the most common variety of mild cognitive impairment causes memory problems. In so called amnestic MCI the patient has subjective memory complaints which are corroborated to an informant, abnormal memory function related to age and education norms but essentially normal general function as well as normal activities of daily living are preserved.[2] There are multiple etiologies for amnestic MCI such as degenerative changes of neurons (which most likely lead to Alzheimer Disease), as well as the multiple infarctions of the brain (it can lead to MCI as a premonitory state of vascular dementia).[3] The risk of vascular cognitive impairment and the rate of cognitive decline in cerebrovascular diseases is dependent upon the control of the risk factors for stroke. The risk of developing cognitive impairment after stroke is greatest in those persons with uncontrolled vascular risk factors (arterial hypertension, homocisteinemia, hyperlipidaemia, diabetes mellitus, obesity, smoking, alcohol, etc.). Besides vascular risk factors for the vascular cognitive decline, there are demographic (e.g., age, education), genetic (e.g., family history and specific genetic features) and ischemic lesion-related variables (e.g., type of cerebrovascular disease, site and size of stroke)[4,5]. Evaluation of early signs of cognitive decline is important because many of the risk factors leading to cerebrovascular diseases can be medically managed to prevent severe cognitive impairment. There is a variety of screening instruments that have been evaluated for their

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usefulness in identifying patients with MCI. Among them we mention Mini Mental State Examination (MMSE)[6] and Cambridge Cognitive Examination (CAMCOG). MMSE is most widely used in the assessment of patients with memory complaints, althought it lacks sensitivity in detecting MCI or early stages of dementia. Another brief screening tool with high sensitivity for MCI is CAMCOG. It forms part of a standardized psychiatric assessment schedule, CAMDEX (Cambridge Examination for Mental Disorders of the Elderly), devised by Roth and colleagues and published by Cambridge University Press.[7] It assess a wide range of cognitive functions such as attention, memory, abstraction, language, praxis, orientation and perception. In our study we used both MMSE and CAMCOG to compare the incidence and severity of cognitive decline in patients with first clinical signs of cerebrovascular disease and in subjects with one or more cerebrovascular risk factors, with no clinical signs of cognitive impairment.

MATERIAL AND METHODS

We studied a group composed of 86 patients(mean age 62,02± 6,10 years) and mean level of education of 10,15±2,10 years admitted in The Clinic of Neurology Craiova during the year 2007, for first ever ischemic stroke or TIA and also a group composed of 92 control subjects without clinical signs of cerebrovascular disease but with vascular risk factors present. The control subjects had mean age 62,20±4,30 years and a mean level of education of 10,30±2,23years. None of the study subjects had any subjective or objective memory complaints prior to enrolment. We performed to all patients a CT scan exam for a correct diagnosis. In all control group subjects brain CT scan results were normal, free from any signs of cerebrovascular disease. In all subjects data on conventional vascular risk factors were recorded, including age, arterial hypertension, diabetes, hiperlipoprotaeinemia, smoking, alcohol and obesity, coronary disease and atrial fibrillation. Upon giving an informative consent, both groups (patients and controls) were tested using MMSE and CAMCOG. MMSE is composed of items assessing orientation, immediate and delayed recall of three words, naming, phrase repetition, the ability to follow simple commands, writing, visuospatial function, attention and mental control. Total MMSE score of 25-30 points is considered normal, while scores below 24 points indicate dementia[6]. CAMCOG is a brief neuropsychological battery very useful for detecting mild degrees of cognitive impairment.The maximum overall score is 105. A cut-off of 80 was found to discriminate between demented and normal subjects. Our evaluations were made in the beginning of the study (baseline) than after 3 months respectively 6 months. The results were analysed by Student Test ($p < 0,05$ statistically considerable).

RESULTS

There were 58 ischemic acute stroke patients (67,44%) and 32 TIA patients (37,20%) enrolled in the patients group versus 92 control group subjects with no clinical evidence of cerebrovascular disease but with the presence of one or more risk factors. TIA was diagnosed according to redefined diagnostic criteria of the TIA Working Group[8]. There was no statistically significant difference between groups concerning the age and the level of education. The demographic data are summarized in Table 1. In the control group arterial hypertension was the most frequent risk factor (n= 70; 76,08%), followed by hiperlipoproteinaemia (n=62; 67,39%) and diabetes mellitus (n=45; 48,91%). In the stroke patients subgroup the arterial hypertension (n=45; 83,37%) was most commonly recorded, followed by hiperlipoproteinaemia (n=37; 68,51%) and smoking (n=30; 55,55%). In the TIA patients subgroup hyperlipoproteinaemia (n=28; 87,50%) was most commonly recorded, followed by arterial hypertension (n=20; 62,50%) and atrial fibrillation (n=16; 50,00%).Also multiple risk factors were present in 29 (53,70%) stroke patients versus 14 (43,75%) TIA patients. (Table 2).

Table 1. *Study subjects demographics*

	Number of patients	Age (years)	Education (years)
Patients group	86	62,02±6,10	10,15±2,10
Stroke group	54	60,03±5,90	10,51±2,58
TIA group	32	64,15±3,18	11,90±3,01
Control group	92	62,20±4,40	10,30±2,23

Table 2. *Vascular risk factors in TIA subgroup, stroke subgroup and control group*

	Transient ischemic attack subgroup(N=32) n%	Stroke subgroup(N=54) n%	Control group(N=92) n%
Arterial hypertension	20(62,50%)	45(83,33%)	70(76,08%)
Hiperlipoproteinaemia	28(87,50%)	37(68,51%)	62(67,39%)
Diabetes mellitus	15(46,87%)	21(38,88%)	45(48,91%)
Smoking	15(46,87%)	30(55,55%)	42(45,65%)
Atrial fibrillation	16(50,00%)	22(40,74%)	36(39,13%)
Obesity	10(31,25%)	19(35,18%)	32(34,77%)
Multiple risk factors	14(43,75%)	29(53,70%)	39(42,39%)

- **The cognitive results using MMSE scale**

In patients group we found at baseline a mean score 27,3; after 3 months the mean score was 26,3 and 6 months later 25,4. The control group obtained at baseline a mean MMSE score 28,5; after 3 months 27,6 ; and in the end of study 26,6. The values are represented in figure1.

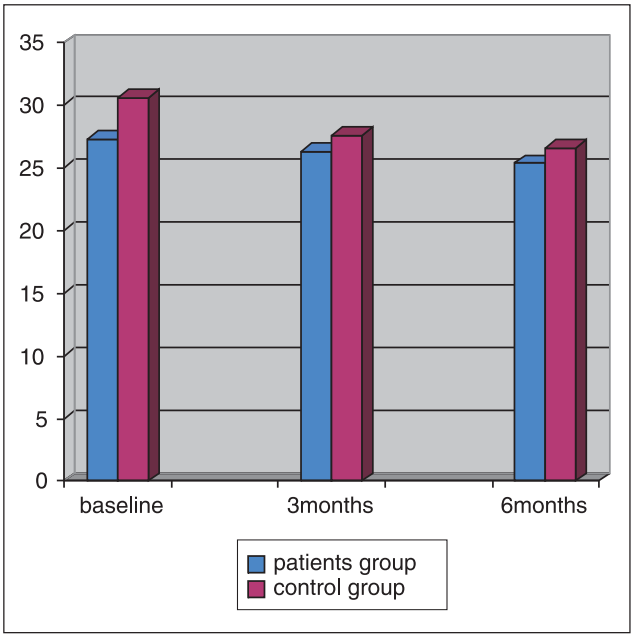

Figure 1. *Mean MMSE score in patients group and control group at baseline, after 3 months and after 6 months*

- **The cognitive results using CAMCOG test**

In patients group we found at baseline a mean score 93,9; after 3 months the mean score was 87,9 and 6 months later 81,9. The control group obtained at baseline a mean score of 96,8; after 3 months 92,6 and in the end of study 88,95. The values are represented in figure 2. As shown in figures 1 and 2, cognitive performance on MMSE for both groups fell within the normal range throught the study period and the administration of CAMCOG revealed early cognitive abnormalities : after 3 months in the patients group and after 6 months in both groups (patients and controls). We have also observed using assessment by CAMCOG that the patients group showed a higher cognitive impairment in comparison to the control group ($p < 0,05$) after 6 months. When we used CAMCOG we observed that the stroke patients subgroup who had multiple vascular risk factors(n=29; 51,78%) had a statistically significant cognitive decline after six months (mean CAMCOG score 80,04) in comparison to TIA patients subgroup (n=14; 43,75%) with a mean CAMCOG score of 89,7 points. As shown in figure 3, in control group the greatest cognitive decline at 6 months was recorded in the subgroup of subjects with arterial hypertension (mean CAMCOG of 85,76) and multiple vascular risk factors (mean CAMCOG 83,24).

DISCUSSIONS

Cerebrovascular disease and dementia are among the most common diseases in aging societies. Cognitive disorders after stroke are one of the main causes of disability in daily activities.The patients with MCI have an increased risk of developing Alzheimer Disease over the next few years, especially when their main problem is memory. There are opinions that essentially all cases of MCI progress to Alzheimer Disease or another form of dementia, therefore MCI is an early sign of dementia. Other opinions suggest that some people with MCI may not develop dementia. It is considered also that there are people diagnosed with MCI who may return to normal. Patients with MCI should be recognized and monitored for cognitive and functional decline due to their increased risk for subsequent dementia.

The results of our study indicated that first measurable signs of cognitive impairment appear before the disease itself had become clinically evident. The cognitive assessment using CAMCOG

during a 6 months period in group of patients and controls too, showed a cognitive decline in both groups. It was observed a more pronounced decline in the patients group comparatively with the control group (Fig 2). There are several studies which have

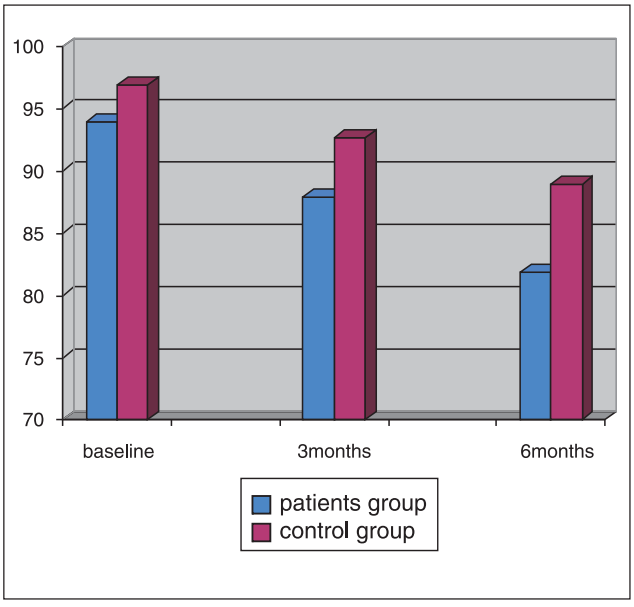

Figure 2. *Mean CAMCOG score in patients group and control group at baseline, after 3 months and after 6 months*

suggested that the vascular cognitive decline is strongly associated with the cerebrovascular risk factors. The common risk factors for Alzheimer Disease and vascular dementia are considered age, arterial hypertension, diabetes mellitus, smoking, hiperlipoproteinaemia, coronary heart disease or previous TIA or stroke[9,10]. The recent epidemiological and experimental studies showed that there are many reasons to consider the role of vascular factors in the initiation and progression of Alzheimer Disease. As vascular pathology is common in both vascular dementia and Alzheimer Disease, in our opinion the early detection of MCI is very important, especially in the patients to whom medical control of risk factors could prevent clinically evident dementia of any type. In this context, we have observed in our study that CAMCOG can detect discrete cognitive changes in symptom free subjects with no cognitive complaints but with one or more risk factors (Fig. 2). Using CAMCOG for the assessment of patients group, we obtained a higher cognitive decline after 6 months in comparison to baseline and 3 months follow-up period. Also we observed that the ischemic stroke patients subgroup had a higher cognitive decline than TIA patients subgroup. Using MMSE we obtained signs of cognitive decline in patients group after 6 months, while no abnormalities were found in control group (Fig. 1). In the control group we observed a discrete cognitive decline, especially in control subjects with arterial hypertension and multiple vascular risk factors (they had the most pronounced decline after 6 months) (Fig. 3). It appears that the concurrent

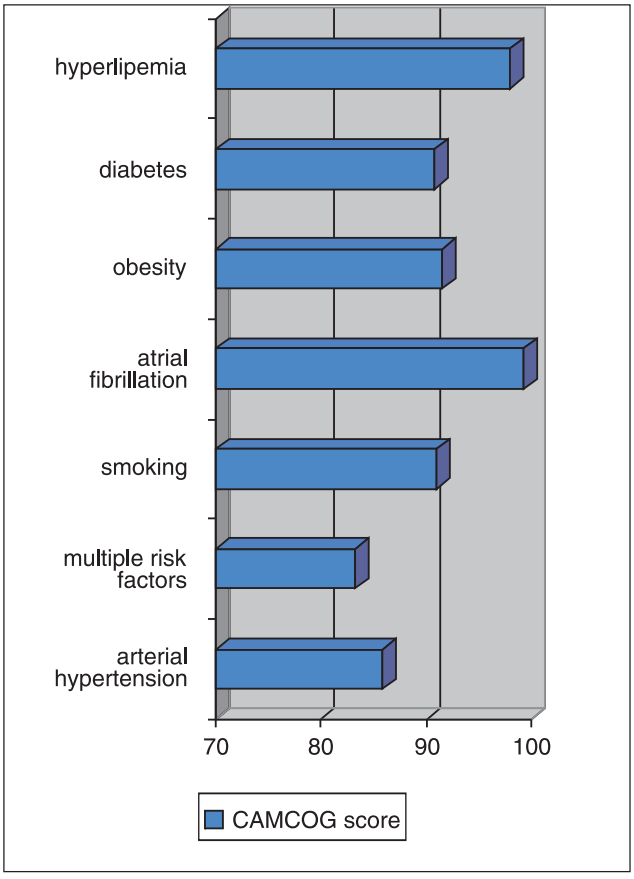

Figure 3. *Mean CAMCOG score in control group according to risk factors at 6 months*

presence of multiple vascular risk factors additionally increases the risk of subtle cognitive decline through possible cumulative actions of risk factors even in subjects without evident clinical signs of cognitive impairment.

Our results are in concordance with other studies that observed MMSE could not be used alone to diagnose MCI or dementia[11] . We demonstrated that the utilization of CAMCOG is very useful for the early recognition of subtle cognitive impairment in apparently mentally healthy individuals. We consider that CAMCOG can be used in patients with normal MMSE score in order to detect the individuals in presymptomatic stage earlier, therefore we could prevent clinically evident dementia.

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